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Near infrared spectroscopy of a heterogeneous turbid system containing distributed absorbers

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ABSTRACT

In most biological tissues, absorbers such as blood in the blood vessels are localized within a low-absorbing background medium. To study the effect of distributed absorbers on the near infrared reflectance, we developed a Monte Carlo code and performed time-domain measurements on heterogeneous tissue-vessel models. The models were made of low absorbing polyester resin mixed with TiO_2 as scatters. A series of tubes with diameters of 3.2 or 6.4 mm were made in the resin sample. The volume ratio of the tubes to the total sample is about 20%. During the measurement, these tubes were filled with turbid fluids with different absorption coefficients to simulate blood in various oxygenation states. We found that the apparent absorption coefficient of the resin/tube system, determined by using the diffusion equation fit, can be approximated by a volume-weighted sum of the absorption coefficients of the different absorbing components. This approximation has to be replaced by a more complex expression if the difference in absorption between the absorbers and background is very large (~ 20 times). The results of the tissue phantom study are supported by the Monte Carlo simulation. Possible explanations for the photon migration in this kind of heterogeneous systems are also presented.

1. INTRODUCTION

In recent years, researchers have developed near infrared (NIR) techniques, including steady-state, time-domain, and frequency-domain measurements, to monitor the brain oxygenation non-invasively.[1,2,3,4] In particular, NIR time- or frequency- resolved spectroscopy has a great potential to determine an absolute oxygenation state of cerebral blood and tissue since these techniques can measure accurately absorption coefficients and path lengths.[5] However, the brain is a very complex biological organ, consisting of various blood vessels and brain tissue. The detected signal in NIR measurements may result from the high-absorbing blood in arteries, veins, and capillaries, embedded in a large brain tissue background. It is known that in the wavelength range of 700-900 nm, the absorption coefficient of hemoglobin is much larger than that of tissue or water.[6,7] Is it reasonable to ignore tissue background absorption? Does the absorption coefficient obtained from the NIR spectroscopy result from blood only or from a combination of blood in the vessels and background tissue?

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In searching for the answers to the above questions, we conducted this study on a tissue-vessel model, with 1) time-resolved Monte Carlo simulation and 2) time-resolved spectroscopy (TRS) in reflectance geometry. Our goal is to investigate the effect of the distribution and sizes of the distributed absorbers on the NIR time resolved reflectance. This study is essential towards understanding the light absorption by cerebral blood in various blood vessels and achieving quantitative brain oximetry.

2. METHODS

2.1 Monte Carlo simulation

We have modified a well-test Monte Carlo simulation[8] to provide time-resolved photon migration in an infinite heterogeneous model, whose cross section is shown in Figure 1. Small tubes are distributed uniformly in a large homogenous medium. The absorption and reduced scattering coefficients of the background and the material filled in the tubes are represented by μ_a(back), μ_s'(back), μ_a(tube), and μ_s'(tube), respectively. Since the large background can act as hemoglobin-free tissue, μ_a(back) is chosen to be relatively small, around 0.05 cm^{-1}. In the simulation, the input parameters are optical parameters, the diameter of the tubes, d, and the tube distribution distance, l. Thus, the volume ratio of the tubes to the total system is known. The output of the simulation is a time-resolved impulse response, at a chosen source-detector separation, ρ. From the simulated data, we can obtain an apparent absorption coefficient, $\mu_{a\text{-app}}$, for the heterogeneous system, using a diffusion theory fit.

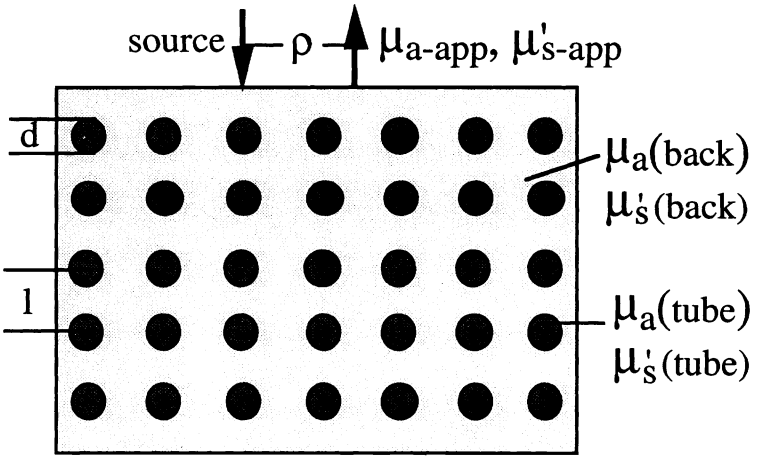

Figure 1. A cross section of a heterogeneous tissue/vessel model for the Monte Carlo simulation. The optical parameters are labeled by μ_a(back) and μ_s'(back) for the background, μ_a(tube) and μ_s'(tube) for the filling material in the tubes, $\mu_{a\text{-app}}$ and $\mu'_{s\text{-app}}$ for the apparent optical parameters for the system.

2.2 Time-resolved reflectance measurements

The absorption and reduced scattering coefficients of a biological sample can be determined using NIR time resolved spectroscopy, and the experimental setup can be found elsewhere.[9] The experimental model for this study is made of a polyester resin, which simulates a low-absorbing tissue background. The resin is mixed with a certain concentration of TiO_2 to obtain a proper value of the reduced scattering coefficient μ_s'(back).[10] As illustrated in Figure 2, a series of small tubes (vertical holes) are made through the resin sample, and they can be filled with an absorbing turbid fluid. The samples used for the

measurements have values of μ_a(back)=0.02--0.06 cm^{-1} and μ_s'(back)=6--9.2 cm^{-1}. The tube diameters in two samples have 3 mm and 6 mm diameters and make up 18% to 20%, respectively, of the entire volume. The measurement was performed on the side of the sample with a separation of 2.5-3 cm at a wavelength of either 670 nm or 780 nm .

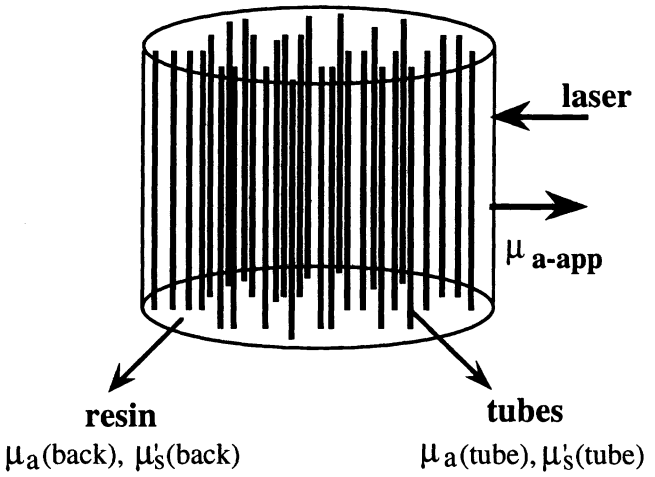

Figure 2. The experimental model made of a polyester resin with many empty tubes simulating the blood vessels. The absorption and reduced scattering coefficients for the filling materials are μ_a(tube) and μ_s'(tube).

To study the dependence of $\mu_{a\text{-app}}$ on μ_a(hole), a set of TRS measurement was performed on the resin sample with an absorbing turbid solution filled in the tubes while increasing the absorption coefficient of the solution. The liquid absorbers in the tubes were either ink or met hemoglobin solutions, the latter of which were made from the hemoglobin (Sigma, H2625) totally converted to met hemoglobin by adding potassium ferricyanide. 0.5% or 1% intralipid was used to dilute the absorbing solutions. The absorption coefficients, μ_a(tube), of the solution at different concentrations were determined separately by taking the TRS measurement on the solution alone. By fitting the TRS spectra taken from the tissue/vessel system with the diffusion theory, we obtained $\mu_{a\text{-app}}$ as a function of μ_a(hole).

2.3 Calculation of the apparent absorption coefficient

In order to study the dependence of the apparent absorption coefficient, $\mu_{a\text{-app}}$, of the system on the μ_a(tube) and μ_a(back), we first assume that the $\mu_{a\text{-app}}$ is a volume-weighted sum of the absorption coefficients of the different absorbing components contained in the medium, as written below:

$$\mu_{a-app} = \sum_i r_i \mu_a(i) \qquad (1)$$

where $r_i = V_i/V_{total}$ is a weighting factor for the *i* th kind of absorbers in the system, and V_i is the tube volume occupied by the *I* th kind of absorbers. When only one kind of absorber is present in the tubes, then equation (1) becomes

$$\mu_{a\text{-app}} = r\,\mu_a(\text{tube}) + (1\text{-}r)\,\mu_a(\text{back}) \qquad (2)$$

With the simulation and experiment in the following, we wish to investigate the validity of equation (2) and to find a suitable formula to express the photon behavior in this kind of tissue-vessel systems.

3. RESULTS

3.1 Simulation results

The empty circles shown in figure 3 are obtained from the simulation with the input parameters of d=4 mm, ρ=18 mm, μ_a(tube)=0.05 cm^{-1}, μ_a(back)=0.5 cm^{-1}, and μ_s'(tube)= μ_s'(back)=10 cm^{-1}. In this case, the system contains only one kind of absorbers. The tubes occupy 34.9% of the total volume, and the background takes 87.4% of the total volume. Then equation (2) gives

$$\mu_{a\text{-app}} = (0.349)\mu_a(\text{tube}) + (0.651)\mu_a(\text{back}) \\ = (0.349)\ 0.5 + (0.651)\ 0.05 = 0.207\ cm^{-1} \qquad (3)$$

On the other hand, the diffusion theory with the values of $\mu_{a\text{-app}}$=0.207 cm^{-1} and μ_s'=10 cm^{-1} gives rise to the solid curve in figure 3. The good consistency between the Monte Carlo simulation and diffusion theory indicates that the apparent absorption coefficient in this kind of heterogeneous system can be approximated by the volume-weighted sum of the composite absorbers. In addition, the solid points in the figure were obtained by changing only μ_s'(tube) from 10 cm^{-1} to 5 cm^{-1}. It is seen that the empty and solid circles are fit with the solid curve nicely. This result suggests that the system is insensitive to the scattering factor of the distributed absorbers, at least if the scattering properties between the absorbers and background are not very large.

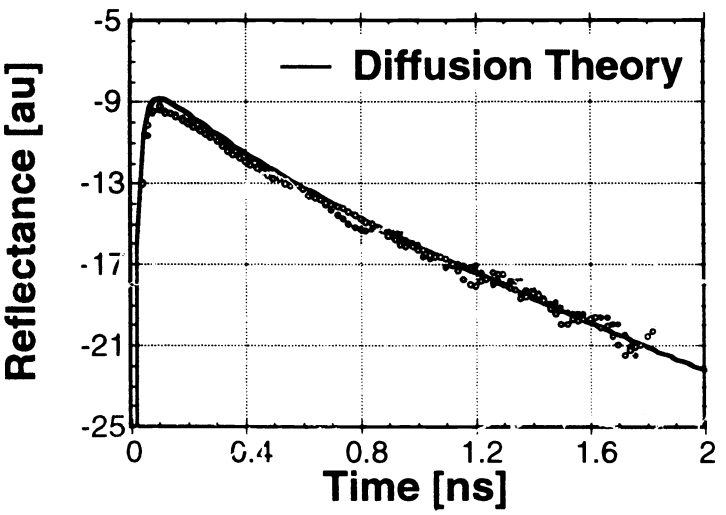

Figure 3. Comparison between the diffusion theory (solid curve) and the Monte Carlo simulation (circles) for a one-kind-absorber heterogeneous system. Empty circles are obtained for μ_s'(tube)=μ_s'(back)=10 cm^{-1}, and solid circles for μ_s'(tube)=5 cm^{-1}, μ_s'(back)=10 cm^{-1}.

We also performed more simulations with different μ_a(hole) values and various volume ratios of the tubes. The numerical results show that the apparent absorption coefficients of the system, calculated from the volume formula of equation (2), can fit the time-resolved reflectance of the tissue-vessel model correspondingly with a little deviations from the diffusion fit only in the earlier part of the time response. When the system contains more than one absorbing component besides the background or the absorption of the absorbers becomes much larger than the background, the deviation become larger.

3.2 Experimental results

The data points in figure 4 show a relationship between the apparent absorption coefficient measured from the system, $\mu_{a\text{-}app}$, and the absorption coefficient of the filling material in the tube, μ_a(tube). In this case, the resin background has a low absorption coefficient of μ_a(back)=0.03 cm^{-1}, and the tubes occupy 18% of the total sample volume. The absorbers were a met hemoglobin solution. The dashed line is based on equation (2) and expressed as:

$$\mu_{a\text{-}app} = 0.18\ \mu_a(\text{tube})+0.82\text{x}0.03=0.18\ \mu_a(\text{hole})+0.025 \qquad (4)$$

It is seen that in the range of μ_a(tube) < 0.25 cm^{-1}, the line fits the data points well; when μ_a(tube) > 0.25 cm^{-1}, the data points start to deviate a little from the straight line.

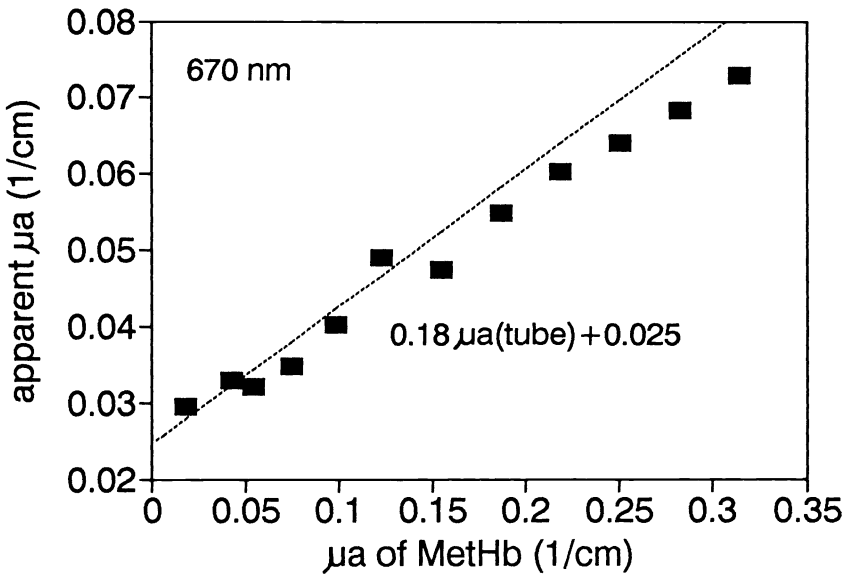

Figure 4. Dependence of the apparent absorption coefficient of the system, $\mu_{a\text{-}app}$, on the absorption coefficient of the met hemoglobin solution inside the tubes, μ_a(tube). 670 nm laser pulser was used in the case. The straight line is given by equation (4).

It seems that the simulation and experimental results support that when the absorption inside the tubes is not 10 times larger than the background absorption, the value of $\mu_{a\text{-}app}$ for a heterogeneous system containing distributed absorbers is proportional to the μ_a(absorber) weighted by the absorber volume ratios; namely, the volume formula of equation (2) is valid. It is known that the absorption coefficient of pure blood is much higher than that of the tissue. By using the Beer-Lambert law, we can estimate the μ_a value (in ln) of human blood at 780 nm by

$$\mu_a^{780} = [c]\ \varepsilon^{780} = 8\ \text{mM}\ 0.46\ cm^{-1}\ mM^{-1} = 3.68\ cm^{-1}$$

where ε is the extinction coefficient of hemoglobin, and it was assumed that the hemoglobin concentration of the blood is 8 mM. The value of 3.68 cm^{-1} is in agreement with our blood measurements using TRS. Therefore, it is useful to study the relationship between $\mu_{a\text{-}app}$ and μ_a(tube) with large μ_a(tube) values.

A similar measurement was performed on the same sample, using an ink solution mixed with 1% intralipid as the filling fuild. But this time, we increased the values of μ_a(tube) up to 4 cm^{-1}. As shown in figure 5 by square points, the measured values of $\mu_{a\text{-}app}$ become very non-linear with μ_a(tube) as the absorption in the tubes are large. The non-linear relationship between $\mu_{a\text{-}app}$ and μ_a(tube) will be further investigated in the discussion section.

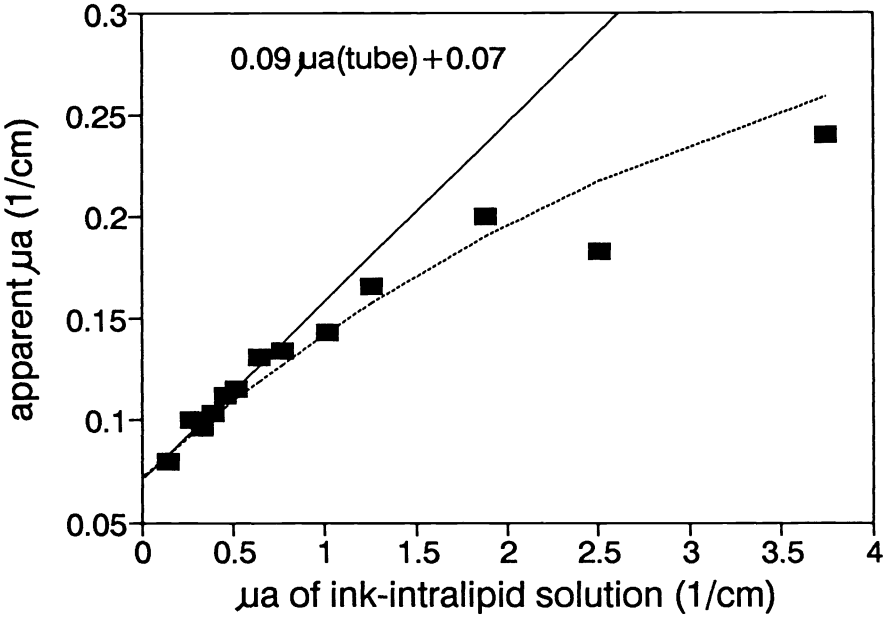

Figure 5. Relationship of the apparent absorption coefficient of the system, $\mu_{a\text{-}app}$, and the absorption coefficient of the ink-intralipid solution inside the tubes, μ_a(tube). In this case, a 780 nm light pulser was used. The straight line is expressed in the insert, and the non-linear dotted curve is expressed in the discussion section.

To study the effect of tube sizes, we took some measurements on two other samples, which have the same tube to total sample volume ratios (20%) but have different tube diameters (3.2 mm and 6.4 mm). The background absorption for these two samples are the same, 0.03 cm^{-1}. Figure 6 presents a comparison of the $\mu_{a\text{-}app}$-μ_a(tube) relationship for these two samples: the solid squares are taken from the sample with 3.2 mm diameter tubes and the plus signs for the sample with 6.4 mm tubes. The results show that the $\mu_{a\text{-}app}$ values obtained from the sample with smaller tubes are larger and remains linear to μ_a(tube) in a larger range than those from the larger tube sample when μ_a(tube) increases. The non-linear relationship between the $\mu_{a\text{-}app}$ and μ_a(tube) in both cases is very clear as μ_a(tube) becomes large.

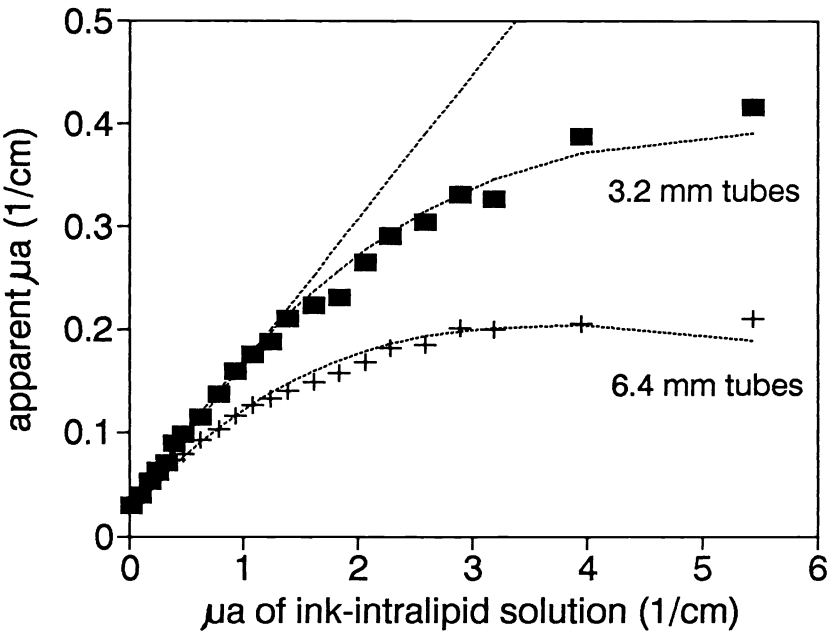

Figure 6. Relationship between the apparent absorption coefficient, $\mu_{a\text{-app}}$, and absorption coefficient in the tubes, μ_a(tube), for the two samples with 3.2 mm tubes (solid squares) and 6.4 mm tubes (plus signs). The solid line is to show the linear relationship between $\mu_{a\text{-app}}$ and μ_a(tube), and the expressions for the dashed curves will be given in the discussion section.

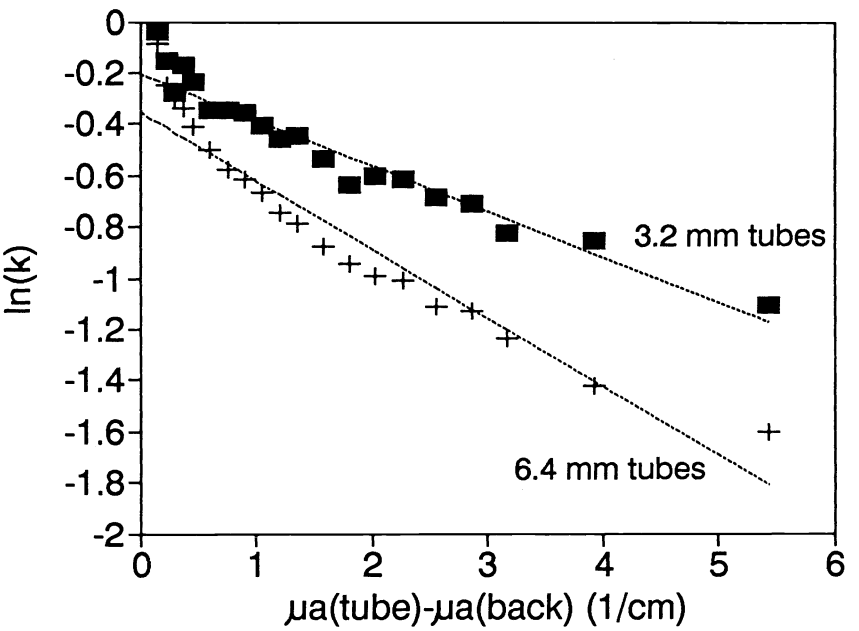

Figure 7. Relationship between ln(k) and [μ_a(tube)-μ_a(back)] for the data given in Figure 6. Solid squares are for the 3.2 mm tube sample with a linear least squared fitting of -0.18x-0.2, and plus signs are for the 6.4 mm tube sample with a fitting expression of -0.27x-0.35, where x is [μ_a(tube)-μ_a(back)].

4. DISCUSSION

In this section, we wish to establish a mathematical formula, based on the above experimental results, to attain an insight into the photon migration in this kind of tissue-vessel models.

For our tissue-vessel model, it is reasonable to express the apparent absorption coefficient $\mu_{a\text{-app}}$ as

$$\mu_{a\text{-app}} = p_1 \mu_a (\text{back}) + p_2 \mu_a (\text{tube}) \tag{5}$$

where p_1 and p_2 are the photon survival probabilities in the background and tube media, respectively. We can also assume that $p_1 + p_2 = 1$. If the two media can be well mixed together, p_1 and p_2 should be equal to the volume ratios of the two media to the total sample. For the tissue-vessel sample, we substitute $p_1 = 1 - p_2$ into eq. (5) and obtain

$$\mu_{a\text{-app}} - \mu_a (\text{back}) = p_2 [\mu_a (\text{tube}) - \mu_a (\text{back})] \tag{6}$$

In order to investigate p_2, we define a factor k in such a way that $p_2 = k\, r_2$, where r_2 is the volume ratio of the tubes to the sample. k may be equal to 1 for two mixable media and depend on both the tube diameters and absorption in the tubes for the tissue-vessel model. Thus, we have

$$k = \frac{\mu_{a-app} - \mu_a(back)}{\mu_a(tube) - \mu_a(back)} \cdot \frac{1}{r_2} \tag{7}$$

Using the data given in Figure 6, we plot ln(k) versus μ_a (tube) - μ_a (back) in Figure 7. It is seen that k decreases as the absorption in the tubes increases; it means that the photon survival probability in the higher absorption medium becomes smaller as the absorption is larger. We can also see that ln(k) has a linear relationship with [μ_a (tube) - μ_a (back)]. The slope of the least-squared fitting to the data points is smaller for the 3.2 mm-vessel sample.

Since ln(k) is approximately linear to [μ_a (tube) - μ_a (back)], we can obtain

$$k = e^{-a[\mu_a(tube) - \mu_a(back)] + b} \tag{8}$$

where a and b are the slope and intercept of the least-squared fitting of ln(k) versus [μ_a (tube) - μ_a (back)], and these two parameters can be determined from the experimental data.

By substituting eq. (8) into eq. (6), we have

$$\mu_{a-app} = \mu_a(back) + r_2 f e^{-a[\mu_a(tube) - \mu_a(back)]} [\mu_a(tube) - \mu_a(back)] \tag{9}$$

where r_2 is the tube to the total sample volume ratio, f is equal to exp(b) and is a constant relating to the sample materials only, and the factor "a" is in proportion to the vessel diameter. Eq. (9) will fall into the volume ratio equation if either the [μ_a (tube) - μ_a (back)] is small or the tube diameter is very small. Based on this equation, we can obtained those dashed fitting curves given in Figures 5 and 6.

In summary, this study shows that the apparent absorption coefficient of a composite tissue/vessel system can be approximately equal to a volume-weighted sum of the absorption coefficients of the different absorbing components if the ratio of $\mu_{a(tube)}/\mu_{a(back)}$ is less than 10. However, with a high absorbing fluid in the vessels, the apparent absorption is affected by both the absorber volume and size, and smaller-size distributed absorbers make a larger contribution to the detected signal in NIR spectroscopy than the larger-size absorbers. Equation (9) suggests that photons have smaller survival probabilities to pass through large vessels since the large vessels absorb the light much more than small vessels and tissue background. The application of equation (9) to brain oxygenation is that NIR techniques may mainly measure capillaries, and that the hemoglobin saturation obtained in the NIR spectroscopy corresponds to the oxygenation of the capillary bed and brain tissue.

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